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AUTHOR Chamberlain, Joyce E.; And Others
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ABSTRACT

The purpose of this study is to present an experimental investigation of the manifestations of aphthous ulcers, glossitis, and cheilosis in the oral cavities of 25 subjects, the use of ferrous gluconate supplements for the control of the lesions in 13 subjects, and the hemoglobin levels at initial and final clinic visits of all subjects for time periods varying from one month to four years. On the basis of the findings and within the limitations posed, it is concluded that: (1) the presence of the oral lesions does not appear to be significantly related to hemoglobin levels, which fall well within the generally accepted normal limits; (2) although hemoglobin levels may fall within the generally accepted normal limits, ferrous gluconate supplements have a profound effect upon reversal of established oral lesions and the prevention of recurrences; (3) hemoglobin levels that are at the lower limits or below the recognized minimum normal range seem to accompany or promote the occurrence of oral lesions; (4) females appear to have a tendency toward occurence of iron deficiency more often than males, and therefore show more frequent manifestations of oral lesions apparently related to the hemoglobin level in the blood; (5) when ferrous gluconate supplements are prescribed for the management of oral lesions, subjects show an increase in hemoglobin determinations, and the majority show marked improvement in the oral conditions following treatment; (6) when ferrous glutonate supplements are not prescribed for the management of lesions, subjects show no improvement; and (7) although the regular intake of iron supplements is not recommended, some subjects require daily supplements. It is recommended that the relationship between nutrition and dental health be amplified in school health programs, expecially in underprivileged urban areas. (DMT)

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The Need of Dental Health Education: Exploring One Aspect of Malnutrition and its Relationship to Oral Health

by

Joyce E. Chamberlain, M.A.H.E.

Dora A. Hicks, Ed. D.

Harold R. Stanley, D.D.S.,B.S.,M.S.

U S DEPARTMENT OF HEALTH, EDUCATION & WELFARE
NATIONAL INSTITUTE OF EDUCATION

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CHAPTER I
INTRODUCTION

Atypical conditions in the oral cavity may not be considered urgent life or death matters, but they do play important roles in the quality of health. The oral cavity is particularly susceptible to nutritional deficiencies, because of the metabolic activities of the epithelial tissues. These are highly specialized tissues, and their sensitivity is noted by Schour and Massler (28).

> The oral tissues have been called the barometer of the state of nutrition of the body. Subclinical states are certainly not rare and from the standpoint of diagnosis, perhaps the most important findings are in the mouth.... The alveolar bone, the gingivae and the tongue reflect the present internal status of the body accurately and quickly.

Need for the Study

This is an era when nutritional factors have appeared to play a significant role in preventive dentistry. Various nutritional inadequacies of the human have been linked with early manifestations of changes which occur in the oral cavity. Schour and Massler (28) and Nizel (25) agree that although the deficiencies of Vitamin A, Vitamin C, Vitamin D and of minerals such as calcium and phosphorous are most evident in tooth and bone development, changes in the gingivae are also noted. These gingivae changes are linked especially with deficiencies of Vitamin C. Deficiencies of Thiamin, Riboflavin,

and Niacin are also known to bring about changes of the gingivae, tongue and oral mucosae, such as anthracosis linguae (Black Tongue), secondary pellagra, periodontal diseases, and other oral lesions.

For a long period of time dentists and physicians have been concerned with oral lesions that appear and reappear in the mouth periodically. They include aphthous ulcers, glossitis, and cheilosis. Numerous articles have been written describing these lesions, prescribing therapy and analyzing causes (7) (12) (25) (27). Some researchers estimate that at least 50 percent or even more of the total population suffer from aphthous ulcers, many more women than men, poverish children and college students with inadequate diets.

Exploring one segment of malnutrition, iron deficiency anemia (a depletion of iron stores) has been found to be very common in the general population (4) (6). Some researchers claim that 50 percent of the population suffers from some degree of anemia. In a recent article in the "Clinical Pediatrics Journal", the author noted that nutritional anemia is one of the most widespread of all health problems according to a ten-state nutrition survey. A high frequency was observed in urban and rural poor children, and in another article there was noted a high frequency among the poor older population.

The epithelial tissues are dependent upon the iron level in the blood to maintain metabolic activities. When iron deficiency occurs, the oral tissues are highly affected. It is recognized that iron deficiency may be evidenced in other areas of the body before it becomes observable in the oral tissues, but when the deficiency does become recognizable in the oral cavity, it is usually because

of iron lack over an extended period of time. According to Coleman, iron stores will be depleted before iron deficiency becomes apparent in the blood. For this reason, an individual may show normal blood level of hemoglobin although iron stores are depleted.

The syndrome that incorporates most of the oral lesions such as glossitis, angular cheilosis, and occasionally aphthous ulcers and dysphagia, has been called Plummer-Vinson Syndrome. Iron deficiency has been suggested as a causal contributing factor in the incidence of these maladies when they occur as the syndrome (8). Sutton's Disease encompasses aphthous ulcers but identifies a much more severe state. The ulcers of Sutton's Disease recur periodically, similarly to aphthous ulcers, but endure for extended periods of time and leave scarring. Primary iron-deficiency anemia has not been suggested as a clinical feature in Sutton's Disease, but may very likely occur as a secondary aspect. It appears that aphthous ulcers, although mildly reminiscent of Sutton's Disease, could be of similar etiology.

Can it be determined that iron deficiency may be a precursor to such oral lesions as glossitis (red, burning tongue), angular cheilosis (cracks in the corners of the mouth), and aphthous ulcers (canker sores)? Can it be shown that when iron supplements are administered, the occurrence of these lesions is controlled or reduced? Therapy with iron supplements in the treatment of the oral lesions has been recorded in medical writing, but references are sparse. Suzman (32), Waldenstrom (34), and Darby (7) have reported using various iron supplements with success when treating patients suffering from the Plummer-Vinson Syndrome.

It seems appropriate that additional research is needed in order to substantiate the importance of iron therapy in the control of manifestations of oral lesions. The significance of oral health in total general health is increased by the multiplicity of benefits. The phonetic value in verbal communication, the esthetic value in human facial expression, the gustatory pleasures and masticatory functions which promote digestive function cannot be denied. Both mental and physical discomfort are endured by adults and children alike when they are afflicted with these oral lesions. The pain and discomfort can lead to behavior changes which can cause serious adjustment problems(31).It is unfortunate that some children so affected have been labeled as mentally retarded or backward because of their physical inability to respond adequately (1)(21)(31).

These conditions in the oral cavity may not be considered urgent life or death matters, but they do play important roles in the quality of the individual's health.

If relationships between hemoglobin levels in the blood and the recurrence and reduction of oral lesions can be established, then the evidence may be used to promote better nutrition, and prevent needless suffering. Knowledge of such preventive and protective measures is basic to effective health education.

Purpose of this Study

The purpose of this study was to present an experimental investigation of the manifestation of aphthous ulcers, glossitis, and cheilosis in the oral cavities of 25 subjects, the hemoglobin levels, and the effects of ferrous gluconate supplements on the control of these lesions in selected subjects.

Therapy offering limited relief in the past include: 1) the topical application of Kenalog in Orabase which is a synthetic steroid ointment possessing anti-inflammatory action and 2) a tetracycline mouth wash.

Vitamin C has been used extensively by some dentists and physicians for the treatment or prevention of these lesions. Some claim success while others do not.

If a relationship can be established between the oral lesions and anemia, then it is hoped that this knowledge gained concerning this segment of malnutrition will become inclusive in the comprehensive health education program.

Definition of Terms

The following terms are defined as their meanings are used in the present study:

Aphthous Ulcers (Figure 1) is a disease characterized by

Figure 1. Aphthous Ulcer on the Lateral Margin of the Tongue

painful oval or round, recurrent, single or multiple necrotizing ulcerations of mucosal tissue with gray membrane, regular margins, and surrounded by bright, discrete, thin erythematous ring. (Further illustration may be seen in Chapter IV, cases 4, 20 and 24.)

Cheilosis (Figure 2) is a lesion that appears as open edges or cracks over the skin on either or both sides of the mouth. They are

Figure 2. Cheilosis of Both Corners of the Mouth.

painful, red, moist and covered by a white film. Surrounding epithelium swells, thickens, and becomes inflamed (29). (Further illustration may be seen in Chapter IV, case 4.)

Cyanmethemoglobin procedure is the method employed in the use of the Bio-Dynamics Colorimeter in order to determine calculations of hemoglobin level, and is considered to have a high degree of accuracy. (13-14). This procedure requires a sample of 15 microliters of blood which is then mixed with a solution containing potassium cyanide, potassium ferricyanide, and sodium carbonate. The

ferricyanide converts the hemoglobin iron from ferrous to ferric state to form an oxidized heme combined with globin to form methemoglobin, which then combines with potassium cyanide to produce the stable pigment cyanmethemoglobin.

Dysphagia is difficulty in swallowing, that is caused by ulceration or hyperkeratosis of the esophagus (29).

Ferrous gluconate is an iron supplement which produces rapid hemoglobin regeneration in patients with iron-deficiency anemia. It is better tolerated than other forms of iron because of its low ionization constant and solubility. It does not interfere with proteolytic or diastatic activities of the digestive system, and will not produce nausea, abdominal cramps, constipation or diarrhea in the great majority of patients (26).

Glossitis is an acute or chronic inflammatory disturbance of the tongue which can become painful, bright red in color and with various degrees of hypertrophy (29). (Illustration may be seen in Chapter IV, Case 4.)

Hematocrit determination is a procedure used to determine the volume of erythrocytes, and thus designate high, normal, or low hemoglobin levels. Hematocrit rates have been universally accepted as a basis for hemoglobin determination (2), (22), (24).

Hemoglobin is an iron-bearing protein which normally occurs in the circulating blood in two forms: oxyhemoglobin, chiefly in arterial blood, and reduced hemoglobin, chiefly in venous blood. Hemoglobin determination is carried out by comparing a fresh sample of blood with a standard set of color representing different

intensities of hemoglobin color. A color index shows the amount of hemoglobin in proportion to the red blood cell count. Under normal conditions the number of red cells in each cubic millimeter of circulating blood remains almost constant. Daily variations of one-half million cells are normal, and greater transient increases may occur during stress. The hemoglobin content, expressed in grams per 100 ml. of blood, normally increases in direct proportion to the rise in erythrocyte count. For production of hemoglobin, an adequate supply of iron is required. When there is inadequate production of hemoglobin, one cause is the failure to include sufficient iron in the diet.

Iron-deficiency anemia is a term used to describe moderate and severe iron deficiency because there is insufficient iron to make normal quantities of hemoglobin.

Kenalog in Orabase is a synthetic corticosteroid which possesses anti-inflammatory, antipruritic and antiallergic action used for temporary relief of symptoms of aphthous ulcers.

Plummer-Vinson's Syndrome is characterized by atrophy of papillae and bald spots on the tongue, pain in the tongue and oral mucosa, difficulty in swallowing, accompanied by mouth ulcers and cheilosis.

Sutton's Disease (Figures 3, 4) is a syndrome which begins as a small, smooth, painful red nodule or plaque which soon ulcerates. The craterlike, painful ulcers are much larger and deeper and heal much slower than aphthous ulcers, and leave scarring (31). (Further illustration may be seen in Chapter IV, Case 14).

Figure 3. Craterlike Ulcer of Sutton's Disease on the Lower Lip

Figure 4. Extensive Ulcer of Sutton's Disease on the Upper Lip.

Tetracycline Mouthwash is primarily bacteriostatic treatment for certain gram-positive, gram-negative organisms, and used as prescription for temporary relief of mouth ulcers (26).

CHAPTER II
REVIEW OF LITERATURE

There are stress periods during life when body iron requirements are increased, existing iron-stores are rapidly depleted, and a deficient diet soon produces iron deficiency. Depletion of iron stores is recognized as the earliest phase of iron deficiency. As iron deficiency occurs, iron stores are exhausted before iron-deficiency anemia appears.

Iron-deficiency anemia is the result of a deficit in available iron, i.e., iron absorbed from the diet plus iron reserves within the body, compared with the individual's iron requirements. It is only when iron depletion has been of long standing that manifestations such as glossitis, angular stomatitis and esophageal adhesions (Plummer-Vinson Syndrome) occur (5).

The object of iron therapy is to provide iron in an available form and in adequate amounts to correct the deficiency (5). The availability of ingested iron is related to its solubility and its reduced state. Ferrous salts are considered to have an absorption rate of 10 to 15 per cent in usual treatments given to anemic or iron-deficient patients, and since they have proved effective at low dosages, they have received wide use.

Ascorbic acid is the one substance which has been shown to increase iron absorption. For this reason, some investigators have

combined iron with ascorbic acid for treatments given. Coleman, et al (5) believe this to be of little practical value however, because of the efficacy of iron alone. Results of adequate therapy are highly predictable, and effectiveness is usually determined most efficiently from the rise in hemoglobin (5). Although blood values return rapidly to normal, iron therapy must be continued for extended periods of time in order to reconstitute the iron stores in the tissues.

As early as 1893 Blankenstein (19) suggested that the significance of iron-deficiency anemia may be important in the diagnosis of lesions of the oral cavity. Suzman (32) in 1933, reported an investigation of the etiology of Plummer-Vinson Syndrome and its relationship to "idiopathic hypochromic anemia". He acknowledged that the relationship between anemia and the syndrome "had always been a subject of contention". In 1938 Waldenstrom (34) expressed concern that the study of so-called hypochromic anemia and symptoms afflicting epithelial tissues had not aroused much interest.

Darby (7) reflected in 1946 that recent interest in vitamin B complex deficiencies as causes of lesions of the buccal tissues had led to the unjustified claim by many investigators that all such lesions were manifestations of vitamin deficiencies. It was claimed that changes in the lingual papillae were specifically due to niacin deficiency, and that glossitis was probably due to chronic niacin deficiency. It was further implied that fissures at the angles of the mouth (cheilosis) were due to riboflavin deficiency, although it had been shown that these lesions may heal after administration of

niacin, pyridoxine or pantothenic acid; or that they may be resistant to treatment with all of the known vitamin B factors. Schour and Massler (28) conclude from their studies of the effects of dietary deficiencies on oral structures that, "The oral manifestations of iron deficiency have been given much less consideration than those of calcium deficiency and merit investigation."

Suzman (32) studied eight cases of Plummer-Vinson Syndrome at the Massachusetts General Hospital over a period of two years. The patients were all women between the ages of 27 and 61. Clinical features manifested by these patients were: burning, red tongue which appeared atrophic, smooth and shiny, with fissures present at the angles of the mouth; and dysphagia (tightness in the esophagus). Six of the patients were found to have hemoglobin concentrations which ranged from 35 to 60 per cent at the initial examination. These six patients were given a prescribed daily treatment of iron with ammonium citrate in concentrations ranging from 3.8 grams to 11.6 grams. Treatments were continued for periods of time ranging from one to two months. Final data were available for four of these six patients whose hemoglobin concentrations were found to have increased from 10 to 30 per cent. Their overall physical conditions were improved, and there was marked improvement in the conditions of the mouth and tongue.

Suzman (32) reported a seventh patient who was found to have marked anemia, and a hemoglobin concentration of only 15 per cent. This patient was given intramuscular administration of 900 mg. of ferric citrate over a period of three days, and then a second administration of 1600 mg. over a period of four days. Twenty days after the

second course of iron, hemoglobin concentration had increased 18 per cent, and marked improvement of the lips and tongue were observed. The eighth patient studied by Suzman died on the sixth day, after the filiform bougie which was used for relief of dysphagis was caught in a fold of mucous membrane, perforated it, and then passed through the esophageal wall.

Suzman concluded that since the administration of large amounts of iron almost invariably relieves the anemia, and usually alleviates the lesions of the tongue and mouth, then a virtual deficiency of iron may play some part in the etiology of Plummer-Vinson Syndrome, anemia, glossitis and dysphagia.

Waldenstrom's studies (34) support Suzman. He reported some clinical observations of symptoms from the epithelial organs " "probably caused by iron deficiency." Waldenstrom observed seven cases, all showing typical Plummer-Vinson Syndrome. All cases were females whose ages ranged from 17 to 52 years. Patients presented symptoms which included fissures at the angles of the mouth, burning and soreness of the tongue, and dysphagia. Blood hemoglobin levels were observed to be between 25 per cent and 60 per cent. Patients who were treated with ferrous lactate from two to seven weeks showed much improvement on subjective symptoms, and hemoglobin values were increased. He never used any treatment other than iron, and always experienced good results.

Waldenstrom reported observations of seven additional cases, all of whom showed typical koilonychia, with or without manifestations of fissures at the angles of the mouth, sore tongue and dysphagia, and with or without anemia. He concluded that it seems very probable that

all of these varying combinations of symptoms in the 14 patients, both with and without anemia, have one common cause: iron deficiency. All cases improved after iron medication.

Darby (7) criticized Waldenstrom's conclusions since he did not demonstrate that his cases were resistant to treatment with the vitamin B-complex. Darby suggested that the patients may have consumed a more adequate diet during the period of iron therapy, and therefore may have overcome a concomitant deficiency through manifestations of glossitis and cheilosis, for the association with hypochromic anemia may have been due to an accompanying deficiency of vitamin B-complex.

Darby (7) attempted to present evidence that atrophic lingual papillae, glossitis and angular fissures which accompany iron-deficiency anemias are often due to the lack of iron alone, and not to the accompanying deficiencies of vitamin B-complex. Darby reported a study of six cases encountered at the Nutrition Clinic of the Department of Medicine of Vanderbilt University Hospital. Patients at the Clinic, especially women, usually present the recurrent oral signs, and other symptoms often diagnosed as "subclinical B-complex deficiency", but they fail to respond to therapy with B-vitamins. It was because of this observation that Darby initiated the study of the cases he reported. The B-complex syrup which he prescribed in some cases contained 25 mg. of niacin, 1 mg. of riboflavin and 3 mg. of thiamine, to 4 cc.

All six cases studied by Darby were women between the ages of 24 and 38. Their hemoglobin levels at the initial visit to the clinic ranged between 8.2 and 12.2 g/100 ml of blood. All cases presented

symptoms of oral disturbance related to Plummer-Vinson Syndrome, including glossitis, cheilosis, and aphthous ulcers. Two patients exhibited diagnostic dysphagia. Patients complained of sore mouth, sore and burning tongue, and fissures at the angles of the mouth. All patients exhibited atrophy of the papillae of the tongue.

In two of Darby's cases, B-complex syrup (4 cc, three times daily) was the first prescription given. After eight to nine weeks there was no improvement in oral conditions of either patient. Patient number one was given the additional prescription of riboflavin (5 mg. daily), and there was no improvement after three weeks. Then, pyridoxine (50 mg., three times daily) was added to this patient's medication and within two weeks the lesions improved. The pyridoxine was discontinued at this time, but fissures at the angles of the mouth reappeared and did not respond to administration of 12 grams of yeast, three times daily. Patients number one and number two were both given 0.3 g of ferrous sulfate, three times daily. Patient number one was given the ferrous sulfate in addition to the B-complex syrup. Patient number two was given the ferrous sulfate in addition to the yeast. Three weeks to one month later, these two patients had no soreness of the mouth, the tongue was normal, and the hemoglobin levels had risen from 10.5 g to 12.5 g. After the iron therapy, both patients remained cured.

In case number three, the prescribed treatment was four mg. of riboflavin administered subcutaneously for four days. Oral conditions remained unchanged. Then, supplements of dried brewer's yeast were prescribed (30 g, three times daily), and after six weeks there

was no change. Treatment with pyridoxine (16 mg. daily) was initiated for one week. There was again no improvement. Yeast therapy was added for a period of two weeks, and still there was no change in oral conditions. Then ferrous sulfate (0.3 g, three times daily) was administered for one month. The hemoglobin level increased from 9.8 g to 14.0 g, and the patient showed prompt relief from the symptoms of Plummer-Vinson Syndrome.

Patient number four was given treatment with 0.3 g ferrous sulfate, two times daily, together with 5 mg. of riboflavin administered three times daily. After one month, the oral lesions had completely healed, and the hemoglobin had increased from 9.3 g to 13.0 g. The diagnosis of this patient had been that of ariboflavinosis, with coexisting iron deficiency. It was thought that the response of oral lesions was due to riboflavin. This case illustrates further the confusion which may arise when two therapeutic agents are used. Darby insisted that agents must be tested separately, if accurate interpretations are to be gained.

The two remaining patients, numbers five and six, were treated with ferrous sulfate (0.3 g three times daily) alone. Treatment was not preceded with administration of B-vitamins in order to determine whether the patient would respond to this agent alone. After one to two months, the patients were completely asymptomatic, and hemoglobin levels had increased from a low of 5.7 g to a high of 13.5 g.

Darby's report of representative cases studied was interpreted by him as indication that iron deficiency alone may be manifested by fissures at the angles of the mouth and glossitis. He believed that

this interpretation was consistent with Suzman's successful treatment of 4 cases of Plummer-Vinson's Syndrome with iron administration, and with Waldenstrom's conclusion that these lesions of the mucosa and the dysphagia are both cured by administration of iron with no other therapy.

Darby acknowledged that these lesions are often confused with the oral signs of B-complex deficiencies, as was evidenced by the therapeutic measures which were first instituted in several of the cases he reported. He continued the study of each of his subjects over a long enough period of time; however, he was seeking to be convinced that the B-vitamin preparations were ineffective, and that the iron therapy alone was effective. Darby did not deny that deficiencies of riboflavin, niacin, or other B complex factors may give rise to glossitis or cheilosis. His emphasis was simply that another cause of these signs is iron deficiency. These findings prompted Darby to initiate the study of the correlation of these oral manifestations and the hemoglobin levels of the general adult population. His assumption was that there was more frequent association of these signs with low hemoglobin levels, than with high hemoglobin levels.

In more recent years, Vogel (33), Jacobs, et al (17), Burton (3), Durovic (8), and Mahili (23) have made references to anemia as a causal factor in the diagnosis of these oral maladies, but there is no extensive or structured review of case studies available such as those conducted by Suzman, Waldenstrom and Darby between 1933 and 1946. At the present time the actual cause of the manifestations of aphthous ulcers glossitis, and cheilosis in the oral cavity, and the recommended therapy for their control remain controversial.

CHAPTER III
PROCEDURES

After the problem was selected and adequately defined, the standard "Project Review Form, Committee on the Use of Human Subjects in Research, University of Florida" was completed and submitted, and approval was given for this experimental investigation. Delimitations and limitations were specified, hypotheses were established, and terms used were defined. All available literature related to investigations of the significance of iron deficiency in the manifestations of lesions of the oral cavity was studied and reviewed as a background for the study.

Selection of Subjects

The investigator accepted appropriate subjects for participation in the present study during the four-year period from February 1970 until March 1974. An extended period of time was required for completion of this experimental investigation because of sporadic availability of appropriate subjects, and the need for continuation of observations over an extended period of time.

Need for additional subjects led to posting of notices in strategic places at six multi-purpose buildings on the University of Florida campus in early 1973. These notices included diagrammatic sketches of the types of oral lesions which subjects may present in

order to be considered as participants. Interested potential subjects were requested to contact the investigator by telephone in order to confirm an appointment with the consulting dentist in the Clinic of Oral Medicine at the College of Dentistry of the University of Florida. Potential subjects were also informed that diagnosis and treatment would be provided for them at no cost, if they were selected for participation in the study. A sample form of the notices which were posted appears as Appendix A.

Approximately 25 volunteer subjects responded to the posted notices. An additional 59 potential subjects were patients who were referred to the dental clinic by practicing dentists and physicians throughout Florida. Each of these 59 patients was examined by the dentist in attendance at the clinic, and screened for possible participation as subjects in the present study. Volunteer subjects who responded to the posted notices were urged to make appointments for their initial screening examination without delay if oral lesions were present, so that clinical observation could be made of the ulcerative stages which are of variable duration. Critical judgment in the ultimate selection of all subjects was made by H. R. Stanley, D.D.S., Chairman, Department of Oral Medicine, and his associates at the dental clinic. As a result of the examinations, it was agreed that a total of 45 subjects could be considered appropriate for participation in the present study.

Attrition of potential subjects occurred because of natural mobility, lack of motivation to return to the clinic after relief of pain or acute symptoms as a result of the initial visit, complications because of other illness involvements, and inability to return

to the clinic because of transportation difficulties compounded by the energy crisis of late 1973 and early 1974. These attritions reduced the final study sample to a total of 25 subjects who remained for inclusion in the experimental investigation.

Each of the 25 subjects selected for participation in the present study was requested to complete and sign three necessary release forms. The investigator defined and explained the study, and informed the subject of the right to withdraw from the project at any time. Both the investigator and the subject signed the University of Florida "Informed Consent" form, a copy of which appears as Appendix B. The subject was requested further to agree to the provisions, and sign the College of Dentistry form, "Photographic and Television Release", a copy of which appears as Appendix C. The subject was asked to sign a third release form which authorized the collection of blood specimens, and use of other technical procedures which may be considered necessary or advisable for diagnosis and treatment. This third release form is a routine inclusion of the official form, "College of Dentistry Admission Record, Shands Teaching Hospital and Clinics, University of Florida", and also includes a brief medical history. All completed forms were filed for official use and record as needed.

Each subject was requested to return to the dental clinic for a reevaluation of the oral condition, preferably after a period of 30 days. At the second visit to the clinic, the subject was informed that another extensive oral examination would be made. A second blood sample would be obtained, and a second hemoglobin level and hematocrit

reading would be determined. The condition of the oral lesions observed at this second visit, and the iron levels in the blood would be compared with the findings of the initial examination, and final assessments would be made.

Selection of Subjects for Therapy

At the initial visit at the dental clinic, each subject was given a complete oral examination by the dental consultant in attendance. Close examination was made for any signs of conditions which could be of such serious nature that further participation by the subject would be unadvised. In other situations, oral tissues may have been traumatized through biting, careless toothbrushing, or use of topical applications such as aspirin or other chemicals which may have caused burns. All such extenuating possibilities had to be eliminated so that there could be assurance that lesions manifested were not due to these causes. Lesions resulting from mechanical causes were not appropriate for purposes of the present study.

Atypical conditions of the oral cavity were assessed according to severity and extent. It was the critical judgment of the attending dental consultant to make the ultimate selection of subjects for subsequent laboratory diagnostic procedures.

Laboratory procedures to which each subject was exposed included a hemoglobin level determination, and a packed red cell (erythrocyte) calculation (hematocrit). The investigator, a registered technologist, procured a blood sample through the finger tip puncture method, and determined the hemoglobin level and the hematocrit reading.

As a result of the initial diagnosis which included integration

of the information obtained from the patient's medical history, the clinical observation of oral manifestations, and the laboratory findings, the oral pathologist determined and selected those subjects who were to receive therapy. A total of 13 subjects was selected for treatment. The primary criterion for selection of subjects who received therapy was the nature and extent of the oral lesions. This selection was made regardless of the hemoglobin level, whether it could be considered normal, low-normal, or iron-deficiency anemia. The hemoglobin level was a criterion of secondary importance in the selection of subjects to receive therapy. It was recognized that the standard designation of hemoglobin level which may be indicative of iron-deficiency anemia remains a controversial issue.

Selection of Therapy

Iron was chosen as the therapy for use in this experimental investigation, primarily because of the encouraging results of earlier studies which were reported in Chapter II, "Review of Literature". Suzman (32) used ferric citrate with success. Waldenstrom (34) used ferrous lactate and reported improvement of the oral conditions of his patients. Darby (7) used Vitamin B-complex preceding treatments with ferrous sulfate, and reported that his patients showed no improvement until iron therapy was administered.

The therapy prescribed by the dental consultant for 13 subjects in the present investigation was ferrous gluconate (320 mg.). Ferrous gluconate was selected as the iron therapy of choice because this supplement demonstrates effects readily, and is known to cause little or no gastric disturbance (25).

Iron deficiency is recognized as a most common dietary deficiency, with the possibility of as much as 50 per cent of the population in many areas suffering from this deficiency (6), (30). The American Academy of Pediatrics has recently urged that children should be fed iron-fortified milk to help prevent the prevalence of anemia in this country (9). The Food and Drug Administration is presently considering a new regulation that could triple the amount of iron supplement now added to bread and flour in order to cope with the reported widespread iron deficiency in the United States (15).

It has been postulated that the oral lesions investigated in the present study are as extensive as in iron deficiency. Since it has been demonstrated that there is a possible relationship between iron deficiency and aphthous ulcers, it seemed logical that more conclusive data are needed and that additional efforts should be made to demonstrate effects on the control of these and other oral conditions through the use of iron therapy.

Determination of Hemoglobin Levels

Initial and final hemoglobin levels were determined by the Bio-Dynamics Colorimeter which employs the cyanmethemoglobin procedure as explained in "Definition of Terms", Chapter I. This procedure provides for calculations of hemoglobin level readings in grams per 100 milliliters of blood. Determination of hemoglobin level in grams per unit volume of blood was considered to be more accurate than that of determinations in per cent, as had been done in similar investigations. When calculations are made in percentages, a normal value representing 100 per cent must be established. Assessment of these

normal values has been made with ranges from 13.5 g to 21.2 g/100 ml (11). For the purposes of this study, it was accepted that the percentage basis could imply a false sense of accuracy, since a single sample of blood could render a hemoglobin reading of a low of 61 per cent or as high as 101 per cent.

Reactions in this cyanmethemoglobin method of hemoglobin determination are fast and stoichiometric. Use of the Bio-Dynamics colorimeter with the pre-bottled and accurately measured diluting substance reduces the chance of error. The colorimeter provides for measuring the color intensity electrically, thus eliminating the possibility of human error through the use of the eyes in varying intensities of natural or artificial light.

The hematocrit was used to determine the volume of erythrocytes, and thus designate high, normal, or low hemoglobin levels. A microcapillary pipet (85 microliters) was filled to the three-fourths level with the subject's blood sample. The pipet was then centrifuged at a standard high speed until maximal packing of erythrocytes was obtained. The level of packed erythrocytes was read on a standard scale, which is calibrated for the 85 microliter pipet. The usual range of values for packed red cells for males is from 40 to 54 per cent, and for females, from 35 to 47 per cent of the total blood sample. If any hematocrit value fell below the established normal values for packed erythrocytes, then iron-deficiency anemia could be suspected.

Collection and Treatment of Data

The participation of 25 subjects in this experimental study

provided the data which are presented for observation, summary, and interpretations. These data were recorded for 13 subjects who were selected by the dental consultant to receive ferrous gluconate supplements during the experimental period; and for 12 subjects who received no ferrous gluconate treatment.

The age and sex of each subject were noted, and individual records were made of the initial and final status of each subject according to: (1) clinical assessments of atypical conditions and types of oral lesions, according to severity and extent as designated by the consulting dentist; and (2) hemoglobin levels determined by the investigator. Additional descriptive data were obtained at the subject's initial visit to the clinic, when the dental consultant requested the subject to describe his present condition in his own words. The dental consultant made notations as the patient described his condition, and appropriate information was later recorded in proper sequence.

All initial and final status data were tabulated and summarized for purposes of comparison and interpretation in April 1974. Determinations of changes in hemoglobin were calculated in grams per 100 milliliters of blood, and assessments of any changes in oral conditions were made in simple descriptive terms.

Individual documentary records for each subject were summarized for inclusion in the findings, and pertinent collective data were presented in table forms for purposes of comparison. Interpretations were made with particular reference to subjects who received and did not receive ferrous gluconate supplements, and the apparent relationships between the hemoglobin level and periodic occurrence and

reduction of oral manifestations of aphthous ulcers, glossitis and angular cheilosis. From the interpretations of data, a summary of conclusions and recommendations was made.

CHAPTER IV
PRESENTATION OF FINDINGS

Data which support this experimental investigation are reported and presented in the present chapter. Findings include the manifestations of aphthous ulcers, glossitis, and cheilosis in the oral cavities of 25 subjects, the effects of ferrous gluconate therapy on the control of these lesions in selected subjects, and the initial and final readings of hemoglobin levels of all subjects possible. The types of oral lesions manifested by the 25 subjects according to sex and age distribution, and the summary of hemoglobin readings together with assessment of oral results are given in table form. Reports of individual case findings and observations for the 25 subjects are presented in descriptive form in order to provide supplementary data inappropriate for tabulation.

Types of Oral Lesions Manifested by the 25 Subjects

In Table 1 is presented a summary of the sex and age distribution of the 25 subjects, and the types of oral lesions manifested at the initial visit to the dental clinic. Inspection of Table 1 shows a predominance of female subjects, a total of 20, which represents 80 per cent of the 25 subjects participating in this experimental study. It is observed that a total of 18 of these female subjects (90 per cent) are within the age-groups not

Table 1

Types of Oral Lesions Manifested by the 25 Subjects According to Sex and Age Distributions

Oral Lesions	Age Groups 13-24 M	13-24 F	25-34 M	25-34 F	35-54 M	35-54 F	55-75 M	55-75 F	Total Subjects
Aphthous Ulcers	1	5	1	1	0	2	0	0	10
Glossitis	0	0	0	0	0	2	0	1	3
Cheilosis	0	0	0	0	0	1	0	0	1
Aphthous Ulcers/ Glossitis	0	0	0	0	0	1	0	0	1
Aphthous Ulcers/ Cheilosis	0	0	0	0	0	2	0	0	2
Glossitis/ Cheilosis	0	0	0	0	0	2	0	1	3
Aphthous Ulcers/ Cheilosis/ Glossitis	0	0	0	1	0	0	0	0	1
Sutton's Disease	2	1	1	0	0	0	0	0	4
Totals	3	6	2	2	0	10	0	2	25

exceeding 54 years. This greater proportion of female subjects presenting oral lesions may have been associated with the greater tendency of females to become anemic during the childbearing years because of the regular loss of blood through menstrual flow. Acceptance of this premise may be justified if it can be shown that the hemoglobin level in the blood is related to the occurrence of the oral lesions.

Further inspection of Table 1 reveals that the type of oral lesion presented by subjects most often was that of aphthous ulcers only, as was manifested by a total of 10 subjects (40 per cent). When additional subjects who manifested aphthous ulcers together with glossitis and cheilosis are included in the designation of subjects presenting aphthous ulcers, the total number of subjects manifesting this type of oral lesion is increased to 14, or 56 per cent of the total 25 subjects.

Report of Case Findings

The clinical features and observations of each individual subject of the total 25 subjects are enumerated on the following pages.

Case 1. A 22-year-old female volunteer first came to the dental clinic on January 30, 1970 with the complaint of a long history of aphthous ulcers. At the time of her first examination, three lesions were observed which were inflamed, and she reported that they were causing her much distress. Laboratory findings showed that the hemoglobin level was 12.0 g/100 ml, and the hematocrit reading was 36.00 per cent (low normal for females).

The treatment recommended was ferrous gluconate (320 mg.) tablets twice each day for 30 days. The subject left the vicinity and did not respond to a letter requesting her to return to the clinic for a second observation. She responded to a telephone call made by the investigator in February 1974, four years later, and she returned to the clinic on March 6, 1974. Oral examination at this second visit revealed a normal oral cavity with no oral lesions. The subject indicated that she had not been bothered with any discomfort for over six months. Her hemoglobin level at this second visit was 15.3 g/100 ml and the hematocrit was 46.0 per cent (high normal range). These findings show an increase in hemoglobin level of 3.3 g/100 ml, and an increase in the hematocrit of 10 per cent. The subject continues to take one iron tablet every three days.

Case 2. The subject was a 22-year-old female volunteer who came to the clinic January 2, 1972 with a history of recurrent aphthous ulcers. At the time of her first examination she presented numberous lesions in the oral cavity, both on and under the tongue. She complained of great distress. Her hemoglobin level was 11.2 g/100 ml, and the hematocrit was 32.4 per cent (below usual normal range). The dental consultant prescribed Kenalog in Orabase for temporary relief of symptoms, and recommended therapy with ferrous gluconate (320 mg.) tablets twice each day for 30 days. She returned to the clinic on February 6, 1972. The oral lesions persisted, and her second hemoglobin reading was 11.9 g/100 ml and the hematocrit was 35.7 per cent. Results of these laboratory tests demonstrated an increase of 0.7 g in the hemoglobin level, and an increase of 3.3 per cent in the hematocrit. In interview, she was

evasive about following instructions for the medications prescribed. She was asked to return to the clinic within two months. She moved away from the vicinity before she made the third visit to the clinic. In January 1974 she was sent a letter requesting her to return to the clinic. She did not respond, and a telephone call was placed to her Palm Beach residence. She indicated that her condition was no better, and that her hemoglobin level was "below normal" in September 1973. She stated that she was no longer following the iron therapy prescribed for her at the dental clinic. No further information was available from this subject.

Case 3. The subject was a 24-year-old male volunteer who came into the dental clinic on October 30, 1974, complaining of having suffered almost continuously from aphthous ulcers for several years. At the time of his initial oral examination, two small lesions were observed which he said were causing him distress. His hemoglobin level was 15.0 g/100 ml and his hematocrit was 42.0 per cent (low normal range). The dental consultant recommended that he take one ferrous gluconate (320 mg.) tablet three times a day for 30 days. He returned to the clinic November 27, 1973 with no oral lesions, but stated that he had endured recurrence of one ulcer since his last visit. His hemoglobin level at this second visit was recorded at 15.5 g/100 ml and the hematocrit was 44.0 per cent. These laboratory results revealed a 0.5 g increase in the hemoglobin level, and a 2.0 per cent increase in the hematocrit, which is considered well within normal limits. He was asked to return to the clinic within 60 days. He did not respond to the letter sent to him in January 1974. A telephone call was made to him in late February. He indicated that he was better, and that he did not have the oral lesions as often. The investigator was unable to procure another hemoglobin determination.

Case 4. This subject was a 31-year-old female volunteer who reported to the clinic on April 11, 1973, complaining of manifestations of aphthous ulcers (Figure 5), glossitis (Figure 6), and Cheilosis (Figure 7).

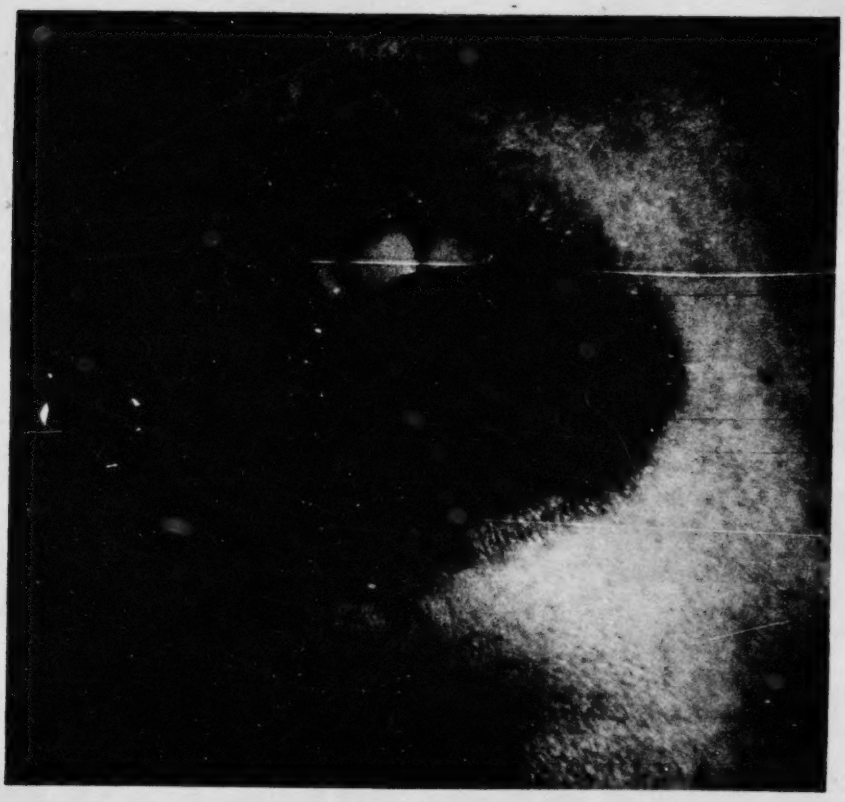

Figure 5. (case 4). Aphthous Ulcer on Oral Papilla of Stensen's Duct

Figure 6. (case 4). Beefy-red Tongue of Glossitis with Angular Cheilosis

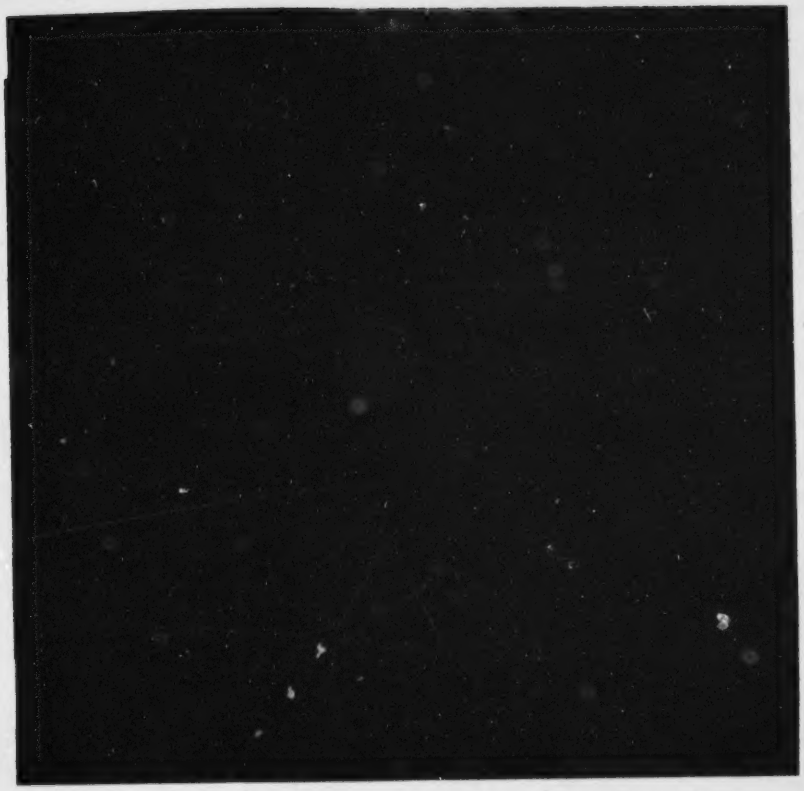

Figure 7. (case 4). Close-up View of Angular Cheilosis

During the oral examination several aphthous ulcers were observed which appeared ulcerated and inflammed. She complained that her tongue was burning. She had deep angular lesions at the corners of her mouth. The subject reported a history of miscarriages, and in March 1973 her physician had diagnosed anemia. She stated that she frequently suffered from these oral lesions. Her hemoglobin level at this first visit was 12.5 g/100 ml. There was no hematocrit determination.

Ferrous gluconate (320 mg.) tablets were prescribed three times a day for 30 days. She returned to the clinic on May 7, 1973. She presented no lesions, and reported that she had not felt so well in years. Her hemoglobin level was 15.0 g/100 ml, demonstrating an increase of 2.5 g. This subject may have endured iron-deficiency anemia since she showed what can be considered a high intake of iron during the 30 day period of the ferrous gluconate therapy. Although her first hemoglobin level of 12.5 g/100 ml could be considered within normal limits, according to some standards, the rapid uptake of iron and prompt disappearance of the oral lesions could indicate that the hemoglobin level was sub-normal for her, and that she did indeed present a mild case of anemia. Further, when these findings are compared with those of case 3, we find that the initial hemoglobin level was considered high at 15.0 g/100 ml, yet when the same therapy was prescribed for him over the same period of time, the hemoglobin increase was only 0.5 g. This confirms previous studies that show that a subject who has a higher normal hemoglobin level will absorb iron at a much slower rate (11), (18).

Case 5. The subject was a 32-year-old female referral who first came into the clinic October 1, 1973 with a two year history of Sutton's Disease. She presented multiple lesions of the tongue, lip, and palate. She indicated that they were so painful that they had affected her personality. She had become irritable and depressed. Her hemoglobin level was 11.5 g/100 ml at the initial visit to the clinic. There was no hematocrit determination at that time. The treatment recommended was Tetracycline mouth wash and Kenalog in Orabase for immediate temporary relief of symptoms. The dental consultant recommended ferrous

gluconate (320 mg.), one tablet twice each day, and requested that she return to the clinic within 30 days. She failed to return, and a letter requesting her to do so was sent in January 1974. She returned to the clinic on January 23, 1974. Oral examination at this second visit revealed one small lesion which was healing. The subject indicated she felt much better, had experienced fewer and smaller lesions and they had healed more promptly than previously. Her husband remarked to the dentist that her personality had improved. Her hemoglobin level at this second visit was 13.8 g/100 ml, and her hematocrit was 42 per cent (normal). It was recommended that she continue the ferrous gluconate treatment, and reduce the quantity to one tablet daily.

Case 5 was the only case of Sutton's Disease for which ferrous gluconate was prescribed in this study. During the three-month period of observation, the hemoglobin was raised 2.3 g, and great improvement was seen in her oral condition. These findings seem to indicate that she may have suffered from iron-deficiency anemia.

Case 6. The subject was a 33-year-old female who was referred to the dental clinic from the Watson Clinic in Lakeland, Florida on January 17, 1972. She presented a two-year history of aphthous ulcers. Several lesions were observed at this first visit. The investigator was not present to procure blood for hemoglobin determination. It was recommended that she use Tetracycline mouthwash and Kenalog in Orabase for temporary relief of pain. The dental consultant prescribed ferrous gluconate (320 mg.) treatment, one tablet twice each day for 30 days. The subject reported by telephone on February 1, 1972 that all lesions

were healed. She had experienced one small lesion which she aborted with Tetracycline mouthwash and Kenalog in Orabase. In January 1973 the subject reported again that she was grateful for relief of pain and symptoms. She indicated she would continue the ferrous gluconate therapy because the lesions would recur without it.

Case 7. The subject was a 36-year-old female referred to the dental clinic by a dentist in private practice in Gainesville, Florida, on May 6, 1971. She reported a one-year history of aphthous ulcers and cheilosis. At the initial oral examination she presented lesions under the tongue, and cracks at the angles of the mouth. Her hemoglobin level was 12.0 g/100 ml recorded at the J. Hillis Miller Health Center. There was no hematocrit procured. The treatment recommended was ferrous gluconate (320 mg.), one tablet twice each day. She was asked to return to the clinic after five days. She visited the clinic on May 11, 1971, and no improvement was noted in the condition of the aphthous ulcers. The cheilosis was improved. She returned to the clinic again on June 7, 1971, and presented no symptoms of ulcers or cheilosis. A letter was sent to her on January 21, 1974 asking her to return to the clinic. She reported on March 20, 1974. She stated that she felt so well that she thought it was a waste of time to continue her visits to the clinic. All oral tissue was normal. Her hemoglobin level at this last visit was 13.5 g/100 ml.

Case 7, whose hemoglobin level was 12.0 g/100 ml at the initial visit to the clinic, could be considered to have presented a hemoglobin reading within normal limits for her. However, after the ferrous gluconate therapy, the hemoglobin level was increased by 1.5 g and the condition of her oral cavity was normal. Need for additional iron

seems to have been indicated by the findings.

Case 8. This subject was a 38-year-old female who was referred to the dental clinic on June 14, 1971 by a dentist in Dade City, Florida. She reported a 15-month history of glossitis. At the initial examination she complained that her tongue and throat burned and hurt, and that she had difficulty in swallowing. Her hemoglobin level was reported to be 12.2 g/100 ml, according to a recent laboratory report. The dental consultant recommended ferrous gluconate (320 mg.) therapy, one tablet twice each day. She returned to the clinic on June 28, 1971 showing no improvement. A letter was sent to her in January 1974, requesting a return visit. She reported by telephone that there was no improvement in her condition, but she failed to return to the clinic. A second hemoglobin level determination was not made.

Case 9. The subject was a 44-year-old female who was referred to the dental clinic on October 15, 1970 with a two year history of manifestations of glossitis and aphthous ulcers. She reported that she had also had ulcers in the vaginal area. Oral examination at the first visit revealed a fiery-red mucosa and tongue. She reported that she had no vaginal lesions at the present time. The subject complained that she could not eat or use straws because of the pain. She reported that she had difficulty in swallowing. Ferrous gluconate (320 mg.) was recommended, one tablet three times each day. A biopsy of the inside lower lip was recommended, if this therapy failed. The hemoglobin level at this first was 12.0 g/100 ml. Her second visit was made on April 2, 1971, and she demonstrated marked

improvement. She had taken the three ferrous gluconate tablets each day for two weeks, experienced marked improvement, and continued the terapy for two months. At this time she reduced the intake to one tablet each day for a period of 30 days and remained free of lesions. The mouth became sensitive again, and oral lesions reappeared. She increased the ferrous gluconate supplement to the original prescription of three tablets each day. She made her last visit to the clinic on February 25, 1974 in response to the followup letter sent to her in January 1974. The subject had no oral lesions present at this time, and reported that she had been free of symptoms for three years. She continued the ferrous gluconate therapy regularly, taking one tablet each day, and increasing the quantity to two tablets each day for four days during the period of menstrual flow. The hemoglobin level at her last visit was 13.5 g/100 ml, showing an increase of 1.5 g.

It is noted that case 9 is another subject whose hemoglobin level at the initial visit could be considered within normal limits for her, and who demonstrated marked improvement in the oral condition, and rise in the hemoglobin level with the ferrous gluconate therapy. It is noted further that therapy had to be continued regularly in order to prevent recurrence of symptoms.

Case 10. The subject was a 45-year-old female who came to the dental clinic on February 13, 1970 with a history of cheilosis. Oral examination confirmed the diagnosis of angular cheilosis. The hemoglobin level at this first visit was 11.0 g/100 ml. There was no hematocrit taken. Ferrous gluconate (320 mg.) therapy was recommended,

and the subject was instructed to take one tablet daily, with an increase in dosage up to three tablets each day during the period of menstral flow. Her last visit to the clinic was on January 17, 1974. She had no lesions present, and stated that she had learned that she had to continue the iron therapy or her symptoms would recur. The hemoglobin level at this time was 13.8 g/100 ml, showing an increase of 2.6 g over the four-year period.

Case 11. The subject was a 46-year-old female who was referred to the clinic by her dentist on April 23, 1970. She reported a four-month history of glossitis and cheilosis. At this first examination, she complained that she was very tired and sleepy much of the time, that her tongue was sore, and the corners of her lips were cracked. Her hemoglobin level was 15.1 g/100 ml at this initial visit. Ferrous gluconate (320 mg.) therapy was recommended, one tablet three times each day for 30 days. The subject failed to return to the clinic and did not respond to a letter which requested her to do so. A telephone call to her was made in March 1974, and she indicated that she was feeling fine. She was convinced that her oral problems had been caused by rough treatment given her by an oral hygienist. The investigator was unable to procure a second hemoglobin level.

In case 11, the subject may have been accurate in her selfdiagnosis, for her hemoglobin level of 15.1 g/100 ml was of high normal range at the first visit to the clinic. Case 11 was one of the three subjects (cases 3, 11, 20) of this investigation whose hemoglobin level was 15.0 g/100 ml or higher at the first visit to the clinic.

A second hemoglobin level determination may have revealed interesting comparisons of conditions manifested.

Case 12. The subject was a 53-year-old female volunteer who came to the clinic on June 8, 1972 reporting a one-month history of glossitis and swollen lips. The initial oral examination revealed a fiery-red tongue. The hemoglobin level was 12.7 g/100 ml, and the hematocrit was 38.0 per cent. Ferrous gluconate (320 mg.) was recommended, one tablet each day for two weeks. The subject returned to the clinic on July 13, 1972. Her tongue appeared normal but her lips were still swollen. The hemoglobin at this second visit was 13.4 g/100 ml, and her hamatocrit was 40.0 per cent. She returned to the clinic again on January 22, 1974. Her oral condition was normal, and she indicated that she felt well. Her hemoglobin level at this third visit had dropped to 12.0 g/100 ml, and the hematocrit reading dropped to 37.0 per cent. She was advised to resume the ferrous gluconate therapy.

In case 12 it is believed that the tongue condition was probably due to a slight iron-deficiency anemia, since it was rapidly resolved through use of ferrous gluconate supplements. Without the therapy, the hemoglobin level and hematocrit became lower than that which was recorded at the initial visit to the clinic.

Case 13. The subject was a 67-year-old female who was referred to the dental clinic with glossitis and cheilosis of long standing. Her first visit was on April 12, 1971, when she presented a deeply creviced tongue, fiery-red gingiva, and severe cheilosis. She had received previous treatments of vitamin and endocrine therapy. The

hemoglobin level at this first visit was 13.7 g/100 ml, and the hematocrit was 41.1 per cent. Ferrous gluconate (320 mg.) was prescribed, one tablet each day for two weeks. Kenalog in Orabase was prescribed for temporary relief of symptoms. If there was no improvement with the prescribed therapy, a biopsy was recommended as a next procedure in order that a more definite diagnosis could be reached. She returned to the clinic on April 30, 1974. She had reduced the ferrous gluconate supplement to one tablet each day. The hemoglobin level at this second visit was 14.2 g/100 ml, procured at the J. Hillis Miller Health Center. There was no hematocrit determination. The hemoglobin level had increased 0.5 g.

Case 14. The subject was a 13-year-old male who was referred to the dental clinic from the J. Hillis Miller Health Center on March 10, 1970 with a long history of Sutton's Disease. On examination he presented multiple lesions throughout the oral cavity. No hemoglobin level was determined at this first visit. Steroids (prednisone) were prescribed. The subject returned to the clinic on July 7, 1970. At this time he presented one lesion on the lower lip (Figure 8), and other than evidence of poor oral hygiene, he seemed very well. The steroid regimen was continuing, and the subject showed no indication of facial change due to the steroids other than a heavy lip fuzz. It was recommended that he use a soft tooth brush, and that the carious teeth be restored as soon as possible. The hemoglobin level at this second visit was 13.1 g/100 ml. There was no hematocrit determination made. He was requested to return to the clinic if he had any further

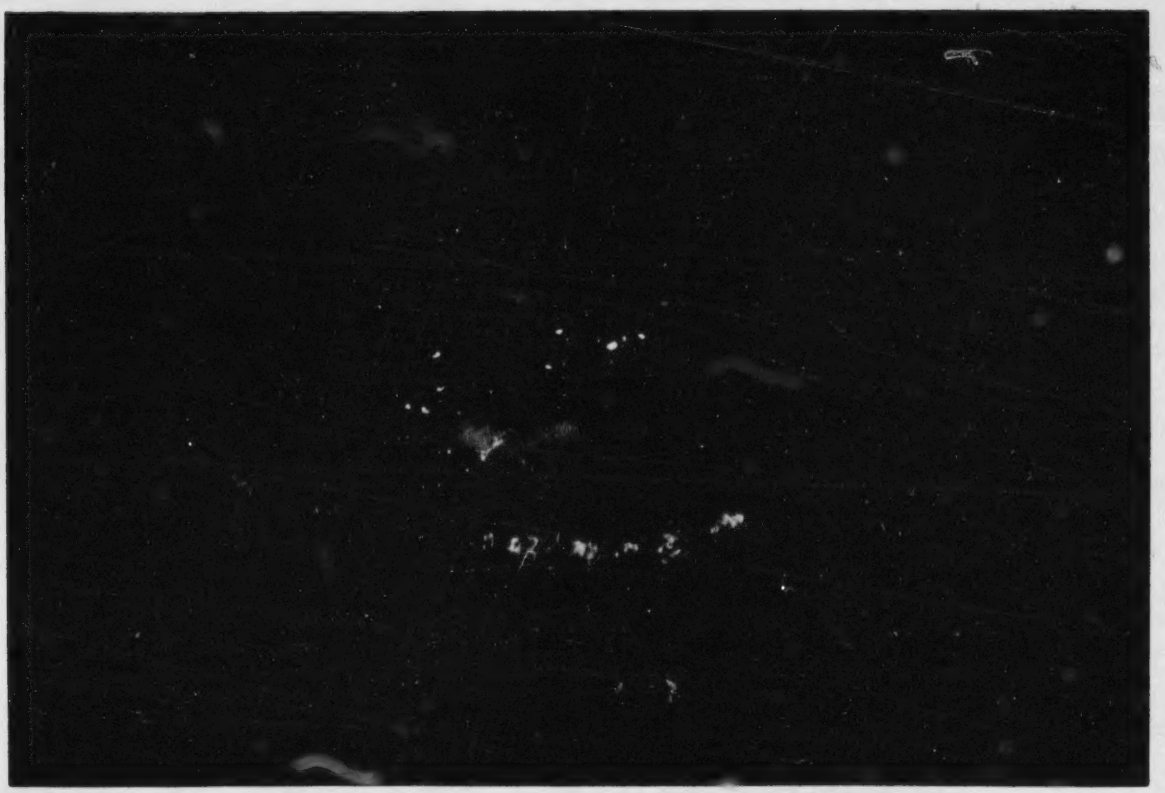

Figure 8. (case 14). Aphthous Lesions Associated with Sutton's Disease

trouble. The subject returned to the clinic on September 14, 1972 with recurrence of Sutton's Disease which he had endured for about two months, following two years of relief. His mouth was still lacking in oral hygiene. He had lesions on the tongue, lips and floor of the mouth. He was continuing the prescribed steroids, and use of Tetracycline mouthwash and Kenalog in Orabase, but none of these seemed to relieve the conditions. He had severe gingivitis, and a mouth that was in a general run-down condition. Scarring was observed. No hemoglobin level was obtained as the patient was much

too ill. Steroids, antibiotics, Tetracycline mouthwash and the use of a water pick were prescribed. The subject returned one week later on September 20, 1972, and examination showed healing lesions. The mouth was in much cleaner condition. The patient was not sent to the laboratory for additional hemoglobin determination. It was recommended that he continue the steroids.

It should be noted that the dental consultant prescribed steroids only because of the judgment that benefits which may be gained exceeded the risks which could be involved.

Case 15. The subject was a 15-year-old female referred to the dental clinic by her dentist. At her first visit on October 6, 1973 she presented a long history of aphthous ulcers. Oral examination revealed three oral lesions, one on the left margin of the tongue, one on the left cheek, and one on the right cheek. The subject reported that she had endured these lesions since she was three years old, with recurrences at least once each month. Her hemoglobin level at this first visit was 13.7 g/100 ml. There was no hematocrit determination. She was given a prescription for Tetracycline mouthwash and Kenalog in Orabase, and requested to return to the clinic after one month. She did not return to the clinic until January 20, 1974. At this second visit, she presented three small lesions. She indicated that she did not like the taste of the Tetracycline mouthwash, and therefore did not use it. The hemoglobin level at the last visit was 12.5 g/100 ml, and the hematocrit was 34.0 per cent. There was a decrease in hemoglobin of 1.2 g.

Case 16. This subject was a 19-year-old male who was referred to

the clinic from the J. Hillis Miller Health Center on November 18, 1971. He reported a five-year history of multiple, deep, and painful lesions of the mouth and of the rectal and anal regions. At an earlier date his physician had prescribed steroids for a brief time. Sutton's Disease was the diagnosis. Oral examination revealed severe aphthous ulcers, and the subject reported that he had endured total mouth involvement. The hemoglobin level at the first visit to the clinic was 13.8 g/100 ml, as had been recorded on the medical record from the J. Hillis Miller Health Center. There was no hematocrit determination recorded. Tetracycline mouthwash and Kenalog in Orabase were recommended for temporary relief of symptoms, and use of a water-pik was recommended for maintenance and cleanliness. The subject was informed that steroids would be prescribed if he showed total mouth involvement again. His mother reported on February 15, 1974 that her son was no better, but that she believed he was no worse. The Hemoglobin level on February 20, 1974 was reported to be 12.9 g/100 ml, according to report from his physician's office in Tampa. This represents a decrease of 0.9 g in the hemoglobin level. Ferrous gluconate (320 mg.) was prescribed at this time, one tablet every day for 60 days. He was requested to return to the dental clinic after this period of time, which was beyond the extent of the present study.

Case 16 presented symptoms of the classic Sutton's Disease Syndrome, and although no improvement or deterioration of his oral condition was reported, it would be interesting to note the outcome of the ferrous gluconate therapy he is presently following.

Case 17. The subject was a 22-year-old female volunteer who reported to the clinic on April 16, 1973. She reported that she had

suffered from aphthous ulcers for as long as she could remember. She presented a giant lesion on the lower left lip. Her hemoglobin level at this first visit was 12.0 g/100 ml. There was no Hematocrit determination. Tetracycline mouthwash and Kenalog in Orabase were prescribed for temporary relief of symptoms. The patient returned to the clinic on February 26, 1974, and presented persistent aphthous lesions. She reported that she took "iron-pills" during the intermittent weeks of taking birth control pills. Her hemoglobin level at this second visit to the clinic was 13.8 g/100 ml, showing an increase of 1.8 g/100 ml during a 10-month period. At this time it was recommended that she take "One-A-Day" iron supplements. She returned to the clinic on April 2, 1974. She presented no lesions, but reported that she had suffered one lesion recently. The hemoglobin level at this third visit was 13.9 g/100 ml showing an increase of 0.1 g over the past month. The hematocrit at this third visit was 38.0 per cent.

Case 18. The subject was a 22-year-old female volunteer who reported a two-year history of aphthous ulcers. She reported to the clinic on November 2, 1973, and examination revealed one lesion on the lower lip. She reported that she had a history of anemia. Her hemoglobin level was 12.5 g/100 ml at this first visit. Kenalog in Orabase was prescribed. The subject reported in January 1974 that she felt better, and that she had no oral lesions. The subject revealed that she had taken oral iron supplements of her own accord. The subject did not return to the clinic for a second hemoglobin determination.

Case 19. The subject was a 29-year-old male who was referred to the dental clinic on March 3, 1973, with a 17-year history of Sutton's

Disease. Oral examination revealed multiple lesions on the lip and deep into the pharynx. The subject reported that he had taken vitamins, and had had smallpox inoculations, but nothing he had done had helped. Several areas of scarring were observed. The hemoglobin level was 14.0 g/100 ml. Tetracycline mouthwash was prescribed. His subsequent visits to the J. Hillis Miller Health Center indicated that he had no permanent improvement. The investigator was unable to contact the subject for a second hemoglobin level.

Case 20. The subject was a 28-year-old male volunteer who first reported to the clinic on June 28, 1972 with a long history of aphthous lesions. Oral examination revealed a deep lesion on his lower lip (Figure 9). The hemoglobin level was 15.0 g/100 ml at this first visit, and a hematocrit of 43.0 per cent. The subject returned to the dental clinic on November 7, 1973. Examination revealed no lesions present at this time, and the subject indicated that he had had no problems for over a year. The subject revealed that his diet had been much improved. His hemoglobin level at the last visit was 16.5 g/100 ml, which shows a 1.5 g increase since his initial visit. The hematocrit was 46.0 per cent at the final visit, showing an increase of 3.0 per cent.

Case 20 indicated that he became aware of the inadequacies of his diet, re-evaluated his eating habits, and proceeded to improve them. He realized that he was not getting enough protein, and "good, red meat". The government food stamp plan had enabled him to improve his eating habits, and thereby improve his oral condition.

Case 21. The subject was a 36-year-old female referred to the

Figure 9. (case 20). Deep Aphthous Ulcer of the Lower Lip

clinic from the J. Hillis Miller Health Center on November 11, 1973, and reporting a seven-year history of aphthous ulcers. Examination revealed three ulcers at her first visit. The hemoglobin level was 12.1 g/100 ml, and the hematocrit was 35.5 per cent. Kenalog in Orabase was prescribed for temporary relief of symptoms. The subject returned to the clinic on May 6, 1974. She indicated that she had no oral problems, and that she had been taking One-A-Day vitamins with iron.

Her hemoglobin level at this second visit was 13.8 g/100 ml, showing an increase of 1.7 g since her last visit six months earlier. Her hematocrit was 40.0 per cent, demonstrating a 4.5 per cent increase.

Case 22. The subject was a 39-year-old female referred to the dental clinic by her physician on October 7, 1971. She complained of having endured aphthous ulcers and cheilosis for long periods of time, and reported that she had both vaginal and oral lesions at the present time. The subject indicated that the vaginal lesions were causing marital problems. She had been taking vitamins for four months but recognized no improvement. The hemoglobin level was 13.0 g/100 ml at this first visit. Her hematocrit was 38.5 per cent. Kenalog in Orabase was prescribed for immediate relief of symptoms. The subject returned to the clinic on October 28, 1971, and three semi-intense aphthous ulcers were observed, one on the lower lip, one on the floor of the mouth, and one on the tongue. She reported that she had one vaginal lesion. The consulting dentist prescribed steroics (40 mg.) for seven days, then a reduction to 30 mg. for one week, a further reduction to 20 mg. for one week, and finally a reduction to 15 mg. to see if her condition would stabilize. Tetracycline mouth-wash was also prescribed. The subject made her last visit to the clinic on April 8, 1974. She presented one very small lesion on the right cheek, and reported that she had suffered no vaginal lesions. Her hemoglobin level at this last visit was 14.1 g/100 ml, and the hematocrit reading was 41.0 per cent. Her overall condition was considered very much improved. The hemoglobin level had increased

1.1 g, and the hematocrit increase was 2.5 per cent. She reported that she felt very well.

Case 23. The subject was a 51-year-old female who was referred by the J. Hillis Miller Health Center on May 3, 1972 with a five-year history of cheilosis and glossitis. On examination she presented a hot, burning tongue and cheilosis. The hemoglobin level was 12.0 g/100 ml. Zinc oxide was prescribed for the cheilosis. The subject returned to the clinic on September 19, 1972, and her oral condition was unchanged. The investigator was unable to obtain a hemoglobin level on the second visit.

Case 24. The subject was a 52-year-old female who was referred to the dental clinic from the Watson Clinic in Lakeland, Florida on November 8, 1972. She presented a history of aphthous ulcers which usually lasted as long as 10 days. Examination showed lesions under the tongue, at the sides of the tongue, and on the upper lip, Figure 10 and 11). The subject reported that she was eating only oatmeal, since everything else hurt her mouth. She had gained 20 pounds within the last year. The hemoglobin level was 14.0 g/100 ml, and the hematocrit was 42.0 per cent. Tetracycline mouthwash and Kenalog in Orabase were prescribed for temporary relief of symptoms. The subject reported next from Lakeland, Florida on November 25, 1972, stating that she still had the ulcers, but that they usually cleared up in three days with the use of Kenalog in Orabase. The investigator was unable to have the subject return to the clinic for hemoglobin determinations.

Case 25. The subject was a 75-year-old female who was referred by the Watson Clinic in Lakeland, Florida on August 2, 1973 with the

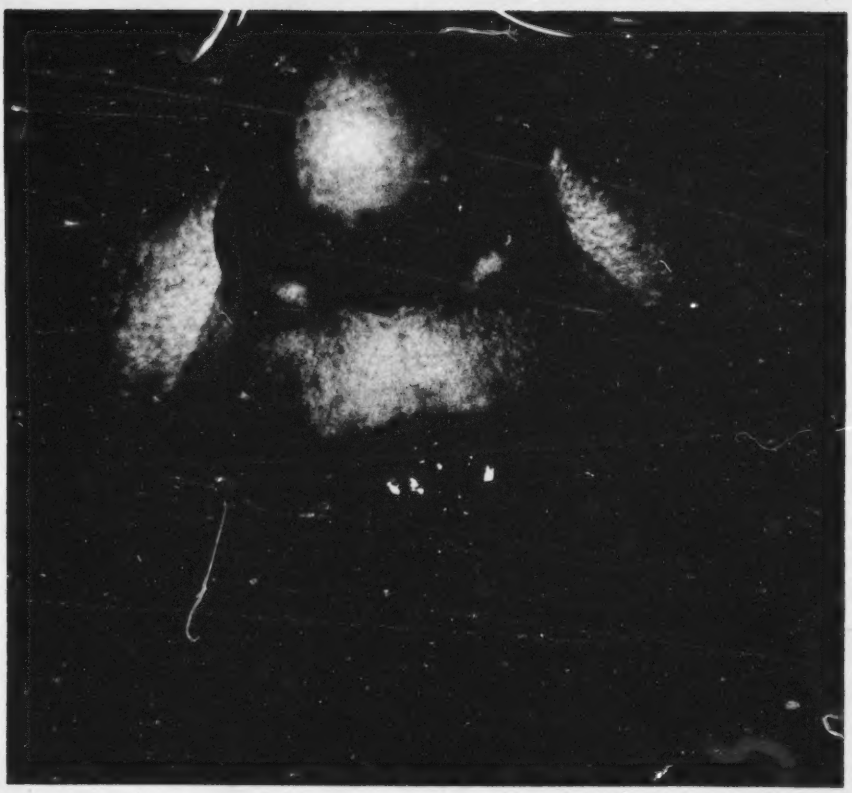

Figure 10. (case 24). Multiple Aphthous Ulcers on the Upper Lip

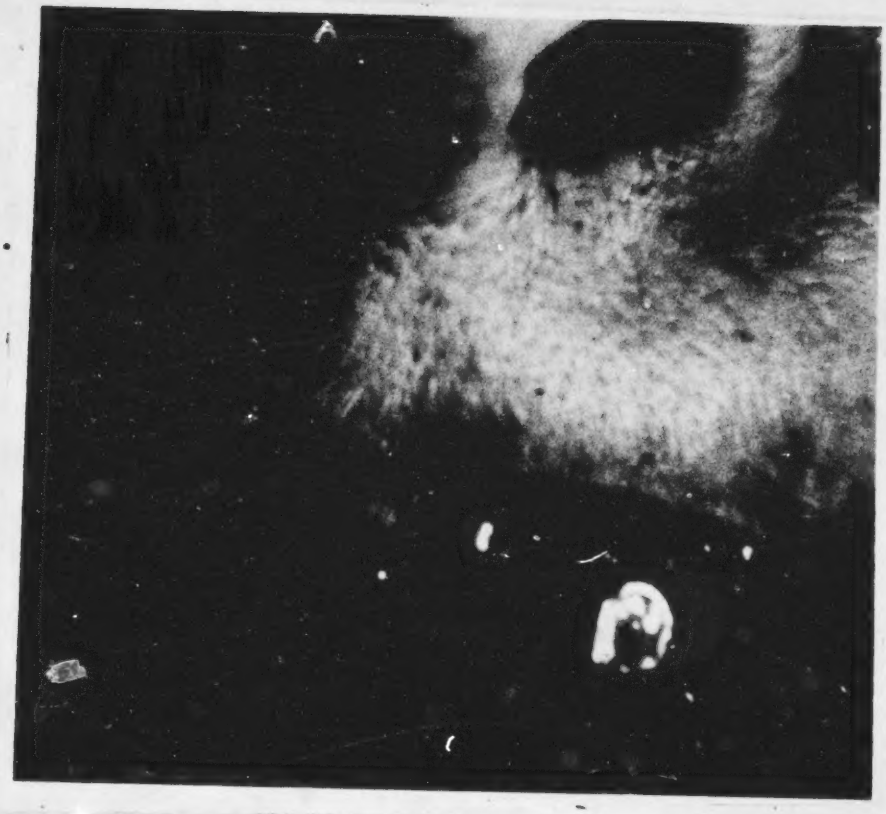

Figure 11. (case 24). Close-up View of Multiple Aphthous Ulcers on the Upper Lip.

record of a long history of hot-burning tongue. Upon examination in the dental clinic her tongue did not appear smooth or atrophic as might be seen in glossitis. The hemoglobin level at this first visit was 12.3 g/100 ml, and the hematocrit was 40.0 per cent. The subject returned to the clinic on March 19, 1974 with the same chief complaint, a burning, hot tongue. The hemoglobin level was 12.3 g/100 ml, the same as it was at the first visit. The subject returned to the clinic on April 18, 1974 appearing somewhat better. She claimed that she felt much better. She had been taking vitamin tablets with iron for the last month, and declared that this was the reason she felt better. The hemoglobin level at this last visit was 13.7 g/100 ml showing an increase of 1.4 g. Her hematocrit at this last visit was 42.0 per cent showing an increase of 2.0 per cent.

This subject was persistent in finding relief from the symptoms although her symptoms were difficult to diagnose during her visit to the clinic. Since the hemoglobin level showed an increase after self-medication of vitamins with iron, a condition of slight iron-deficiency anemia may be considered an underlying cause of her symptoms.

Effects of Ferrous Gluconate Therapy on 13 Subjects

Thirteen of the 25 subjects (cases 1-13) in this experimental investigation were selected to receive ferrous gluconate therapy. Although recording of the hemoglobin level was important for the purposes of the study, it was not a primary factor in the decision of the dental consultant to prescribe ferrous gluconate. The prescribed therapy was in the form of ferrous gluconate (320 mg.) tablets in dosages of one to three tablets daily for a period of 30 days.

The subjects were observed at the dental clinic of the University of Florida during the four-year period of time from February 3, 1970 until April 3, 1974. It may be seen in Table 2 that observations of these subjects extended from a minimum period of two months to a maximum period of 48 months. Although subjects were requested to return to the clinic after 30 days of following the ferrous gluconate treatment, very few complied. Continued encouragement was required to achieve reasonable success in getting subjects to return for a followup check of their conditions. Subjects indicated that they wanted healthy mouths free of disease, pain, and high cost of correction and maintenance. When they were enduring intense pain, no real effort was necessary to encourage subjects to make the initial visit to the clinic. However, once free of immediate pain, the need for a second visit was a remote consideration.

Inspection of Table 2 reveals that atypical conditions exhibited by these 13 subjects at the first visit to the clinic included aphthous ulcers, glossitis, cheilosis, and Sutton's Disease. Five subjects presented combinations of these lesions.

Hemoglobin levels at the first and second visits are recorded in g/100 ml, and the extent of change is indicated in Table 2. It may be noted that the readings of hemoglobin levels at the initial visit of 12 of the subjects ranged from 11.2 g to 15.1 g, with an average reading of 12.59 g. The readings of the hemoglobin levels at the second visit of 10 of the subjects ranged from 11.9 g to 15.5 g, with an average reading of 13.99 g. The change in hemoglobin levels from the initial visit to the second visit of subjects ranged from +0.5 to +3.3 g, showing an average increase of 1.61 g. All subjects for whom

Table 2

Effects of Ferrous Gluconate Supplements on Changes in Hemoglobin and Oral Lesions in 13 Subjects

Case	Age	Sex	Oral Lesion	First Hbg. in G	Second Hbg. in G	Change in Hbg.	Time Observed in Mos.	Improvement
1	22	F	Aphthous Ulcers	12.0	15.3	+3.3	48	Marked
2	22	F	Aphthous Ulcers	11.2	11.9	+0.7	48	None
3	24	M	Aphthous Ulcers	15.0	15.5	+0.5	2	Slight
4	31	F	Aphthous Ulcers/ Cheilosis/Glossitis	12.5	15.0	+2.5	2	Marked
5	22	F	Sutton's Disease	11.5	13.8	+2.3	9	Marked
6	33	F	Aphthous Ulcers	---	---	---	24	Marked
7	36	F	Cheilosis/Aphthous Ulcers	12.0	13.5	+1.5	36	Marked
8	38	F	Glossitis	12.2	---	---	36	None
9	44	F	Aphthous Ulcers/Glossitis	12.0	13.5	+1.5	42	Marked
10	45	F	Cheilosis	11.2	13.8	+2.6	48	Marked
11	46	F	Glossitis/Cheilosis	15.1	---	---	48	Unknown
12	53	F	Glossitis	12.7	13.4	+0.7	36	Marked
13	67	F	Glossitis/Cheilosis	13.7	14.2	+0.5	36	Marked

complete hemoglobin determinations were made showed at least some increase in the level following ferrous gluconate treatment.

Hemoglobin level readings were incomplete for cases numbered six, eight, and eleven. The investigator was unable to procure any hemoglobin determinations for case number six. Cases number eight and number 11 reported oral conditions by way of telephone for the second visit, and did not report to the clinic for a second hemoglobin reading.

It may be seen in Table 2 that the final assessment of the oral condition, which was made by the dental consultant at the final visit, is given in simple terms of improvement. Further examination of Table 2 discloses that nine of the 12 subjects for whom data were available (75 per cent) showed marked improvement in the oral conditions following treatment with ferrous gluconate. The thirteenth subject, case number 11, did not return to the clinic for final evaluation but reported by telephone that she "felt fine".

Two subjects, case number two and case number eight, were the only two cases who showed no improvement in the oral conditions following the ferrous gluconate treatment. In the "Report of Case Findings" it was indicated that there was doubt that case number two followed instructions for medication properly, if at all, since she responded to a telephone call stating that she was not following the iron therapy prescribed for her. Case number eight did not return to the clinic for reevaluation and only reported by telephone that there was no improvement in her condition. One subject, case number three, was reported to have demonstrated only slight improvement in the oral condition. Case number three reported by telephone to the clinic that he did not suffer lesions as often as previously, but

continued to experience them intermittently. It can be seen from Table 2 that the level of hemoglobin for this case could be considered at a high level at the initial visit, (15 g), and after therapy was increased to 15.5 g. Cause for his failure to improve remains in doubt.

Effects of Treatment Rendered to 12 Subjects without Use of Ferrous Gluconate

Subjects numbered 14 through 25 were treated without the use of ferrous gluconate. It is pointed out that the therapeutic management of oral lesions manifested in most of these subjects was attempted through use of Tetracycline mouthwash, Kenalog in Orabase, and in one case, Zinc oxide. Systemic steroids were used in three cases where lesions were "too extensive, too deep, and too numerous, or in areas to which topical steroid ointment cannot be easily applied" (31). It is emphasized that these drugs were given only as temporary medications, since they do not prevent oral lesions from recurring. The drugs do, however, reduce the pain and curtail the length of time during which lesions will persist.

Inspection of Table 3 reveals that the atypical oral conditions exhibited by these 12 subjects at the initial visit to the clinic included six subjects with aphthous ulcers, three subjects with Sutton's Disease, one subject with glossitis, and two subjects with combinations of aphthous ulcers, cheilosis, and glossitis. Hemoglobin levels at the initial visit to the clinic showed a range of 12.0 g to 15.0 g with an average reading of 13.15 g. The hemoglobin levels at the second visit of seven of the subjects for whom readings were

Table 3

Changes in Hemoglobin and Oral Lesions of 12 Subjects
Not Receiving Ferrous Gluconate Supplements

Case	Age	Sex	Oral Lesion	First Hbg./G	Second Hbg./G	Change in Hbg.	Time Observed in Mos.	Improvement
14	13	M	Sutton's Disease	13.1	---	---	47	None
15	15	F	Aphthous Ulcers	13.7	12.5	-1.2	36	None
16	19	M	Sutton's Disease	13.8	12.9	-0.9	45	None
17	22	F	Aphthous Ulcers	12.0	13.8	+1.8	12	Slight
18	22	F	Aphthous Ulcers	12.5	---	---	9	Slight
19	29	M	Sutton's Disease	14.0	---	---	12	Unknown
20	30	M	Aphthous Ulcers	15.0	16.5	+1.5	24	Marked
21	36	F	Aphthous Ulcers	12.1	13.8	+1.7	8	Moderate
22	39	F	Aphthous Ulcers/Cheilosis	13.0	14.1	+1.1	45	Marked
23	51	F	Cheilosis/Glossitis	12.3	---	---	24	None
24	52	F	Aphthous Ulcers	14.0	---	---	2	Slight
25	75	F	Glossitis	12.3	13.7	+1.4	10	Moderate

available ranged from 12.9 g to 16.5 g with an average reading of 14.07 g. The change in hemoglobin levels from the initial visit to the second visit of subjects ranged from -1.2 g to +1.8 g, showing an average increase of 0.77 g. It may be observed in Table 3 that cases numbered 17, 20, 31, and 25 show an increase in hemoglobin levels of 1.4 to 1.8 g. These four subjects reported that they had taken oral iron supplements of their own accord, or that they had received a prescription from their physicians. These supplements may account for the fact that their hemoglobin levels were increased more than those of the other three subjects for whom readings were taken. Hemoglobin level readings were incomplete for cases numbered 14, 18, 19, 23, and 24 since the investigator was unable to secure a second hemoglobin reading.

The final assessment of the oral condition which was made by the dental consultant at the subject's final visit to the clinic is given in Table 3. Time periods during which subjects were observed are shown to extend from a minimum of two months to a maximum of 47 months. It may be observed that only two subjects, case number 20 and case number 22 showed marked improvement in oral conditions, and two additional subjects, cases 21 and 25 showed only moderate improvement. Three of these subjects reported that they had taken oral iron supplements independently, and the fourth subject was prescribed steroids. It is not known whether the three subjects would have shown improvement if they had not taken the oral iron supplements.

Three subjects showed only slight improvement, and two of them, cases 17 and 18, reported that they had taken vitamins with iron

supplements. Four subjects showed no improvement at all, representing 40 per cent of this group of subjects for whom complete data were available, and for whom ferrous gluconate was not prescribed.

It was not possible to contact case number 19 for a final evaluation of his condition.

Hypotheses

It was hypothesized first that the hemoglobin level in the blood is related to the recurrence of such oral lesions as glossitis, aphthous ulcers and angular cheilosis. Those subjects in whom the hemoglobin was increased to a level of 13.4 g or higher, whether or not they received therapy with ferrous gluconate, all showed at least some improvement in oral conditions. Those patients whose hemoglobin levels at the last clinic visit were recorded at 12.9 g or lower showed no improvement in oral conditions.

It has been stated previously that assessment of normal values for hemoglobin has been designated at levels ranging upward from 13.5 g/100 ml. It seems reasonable to conclude that the findings of this investigation support the hypothesis that hemoglobin levels at the lower margin or below the recognized minimum normal range may accompany or promote the occurrence of oral lesions such as glossitis, aphthous ulcers and angular cheilosis. It may be concluded further, that as hemoglobin levels are increased, these oral conditions are improved.

The second hypothesis was that therapy with iron supplements will reduce or control the occurrence of glossitis, aphthous ulcers and angular cheilosis. Data available for 12 of the 13 subjects

who were selected to receive ferrous gluconate therapy show that nine subjects (75 per cent) demonstrated marked improvement in the oral conditions following treatment. Of the other three subjects, there was doubt that one subject followed instructions for the ferrous gluconate therapy; one subject failed to return to the clinic for reevaluation; and the third subject demonstrated only slight improvement. These findings seem to be consistent with those of Suzman (32), Waldenstrom (34) and Darby (7). On the basis of these findings, the hypothesis is accepted.

CHAPTER V
SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Summary

The purpose of the present study was to present an experimental investigation of the manifestations of aphthous ulcers, glossitis, and cheilosis in the oral cavities of 25 subjects, the use of ferrous gluconate supplements on the control of these lesions in 13 selected subjects, and the hemoglobin levels at initial and final clinic visits of all subjects for time periods which varied from one month to four years. The investigation was delimited to a study of subjects who were solicited in the Gainesville, Florida area, or who were referred to the dental clinic of the College of Dentistry at the University of Florida. Selection of subjects was limited to the judgment of the dental consultant who was present in the clinic at the time of the initial visit. His assessment of oral conditions, and selection of therapy prescribed were the final judgments. Determination of the hemoglobin level was made by the investigator, a registered technologist, and was limited to the use of the cyanmethemoglobin procedure.

In order to accomplish the purposes of the study, the following hypotheses were postulated:

1. The hemoglobin level in the blood is related to the occurrence of such oral lesions as glossitis, aphthous ulcers, and angular cheilosis.

2. Therapy with iron supplements will reduce or control the occurrence of glossitis, aphthous ulcers, and angular cheilosis.

Terms were defined as their meanings were interpreted for use in the present investigation. A thorough study and review of related literature was made, and it was revealed that few studies have attempted the investigation of the occurrence of these oral lesions with the possible relatedness of hemoglobin levels, and the effects of therapy with only iron supplements.

Data which support this experimental investigation were provided by the participation of 13 subjects who were selected by the dental consultant to receive ferrous gluconate supplements during the experimental period, and by 12 subjects who received no ferrous gluconate treatment. Clinical, laboratory, and descriptive data were obtained at the subject's initial and final visits. All data were tabulated and summarized for purposes of comparison and interpretation of the findings. Interpretations were made with particular reference to apparent relationships between the hemoglobin level and periodic occurrence and reduction of oral manifestations of aphthous ulcers, glossitis and angular cheilosis.

Conclusions

On the basis of the findings, and within the limitations posed in the present investigation, the following conclusions are made:

1. Presence of the oral lesions of aphthous ulcers, glossitis and cheilosis does not appear to be signiticantly related to hemoglobin levels which fall well within the generally accepted normal limits.

2. Although hemoglobin levels may fall within the generally

accepted normal limits, ferrous gluconate supplements have a profound effect upon reversal of established oral lesions and the prevention of recurrences.

3. Hemoglobin levels which are at the lower limits, or below the recognized minimum normal range seem to accompany or promote the occurrence of oral lesions such as glossitis, aphthous ulcers and angular cheilosis, and as hemoglobin levels are increased, the oral conditions are improved.

4. Females appear to have a tendency toward occurrence of iron-deficiency more often than males, especially during the child-bearing years, and therefore show more frequent manifestations of oral lesions apparently related to the hemoglobin level in the blood.

5. When ferrous gluconate supplements are prescribed for the management of oral lesions such as aphthous ulcers, glossitis and cheilosis, subjects show increase in hemoglobin determinations, and the majority show marked improvement in the oral conditions following treatment.

6. When ferrous gluconate supplements are not prescribed for the management of oral lesions such as aphthous ulcers, glossitis and cheilosis, subjects show no improvement in the oral conditions.

7. Although the regular intake of iron supplements is not recommended, it appears that some subjects require daily supplements until the lesions resolve, and some subjects require daily supplements indefinitely.

In the future, the variances in hemoglobin levels will have to be considered. What may be considered a normal hemoglobin level in an average individual may not be adequate to control oral lesions in an otherwise healthy individual. We don't know what a normal limit is for these individuals. What we do know is that the extra boost with iron therapy brings about relief to these individuals.

Even though this pilot study may be considered inconclusive because of the small sample studied, the results indicate a strong relationship exists between the oral lesion and anemia. Until the consequences have been determined and recorded on larger studies the health educator should be aware that the strong possibility of nutritional anemia exists when the oral lesions are present. This information on dental health should be included in a comprehensive health education program in the schools.

Recommendations

Based on the findings reported in this investigation, the following recommendations are made:

1. The study should be replicated in another geographic area where iron-deficiency may not be encountered as frequently as it is reported to be found in Florida.

2. Additional studies of larger groups of subjects should be conducted, under conditions of more direct control of the prescribed treatments.

3. Similar study should be made of these conditions where all subjects are given double-blind options using iron tablets and similar placebos.

4. Additional studies should be conducted where more extensive hemoglobin determinations and blood analyses are made.

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